Prevalence estimates for chronic urticaria in the United States: A sex- and age-adjusted population analysis

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Background: Disease burden in chronic urticaria (CU) is poorly understood.

Objective: To estimate standardized overall and sex-, age-, and race-specific prevalence estimates for CU among adults in the United States.

Methods: A cross-sectional analysis with electronic health records data for a demographically heterogeneous population-based sample of >55 million patients across all 4 census regions.

Results: The overall CU prevalence was 0.23%, or 230 CU cases/100,000 adults. The adjusted prevalence in women was 310 (95% confidence interval [CI] 307-312) cases/100,000 adults, more than twice that of men (146 [95% CI 143-148] cases/100,000 adults, $P < .001$). CU prevalence was highest among patients aged 40-49 years (256 [95% CI 252-261] cases/100,000 adults) and 50-59 years (246 [95% CI 242-251] cases/100,000 adults) compared with all other age groups ($P < .0001$). Adjusted prevalences for black (292 [95% CI 285-298] cases/100,000 adults) and other (331 [95% CI 323-338] cases/100,000 adults) patients were higher than that for white patients (262 [95% CI 260-264] cases/100,000 adults; $P < .001$).

Limitations: Use of administrative data has the potential to underestimate burden.

Conclusion: There are >500,000 people estimated to have CU in the United States, most of whom are women or adults ≥40 years of age. (J Am Acad Dermatol 2019;81:152-6.)

Key words: burden of disease; chronic urticaria; Explorys; population-based; prevalence; urticaria.

Urticaria is characterized by transient wheals, which might itch or burn or be accompanied by angioedema. Most patients who experience urticaria have acute disease that resolves within 6 weeks. In chronic urticaria (CU), patients experience daily or almost daily wheals, angioedema, or both for at least 6 weeks.[1]

For more than half of patients, symptoms might persist for up to 10 years after initial diagnosis.[2] CU patients experience significant health-related reductions in quality of life. Visible presence of wheals might also lead to emotional upset, causing patients to withdraw from social activities.[3,4] CU patients might also sense a loss of control due to unpredictability of flares.[5] Patients suffer from sleep disturbances, fatigue, and irritability due to pruritus, as well as psychiatric comorbidities including anxiety, depression, somatization, and obsessive-compulsive disorder.[6-9] CU is also linked to socioeconomic burden related to direct health costs[10,11] and loss of work productivity.[12-14]

Although CU results in significant morbidity, the overall burden of disease is poorly understood. The purpose of this study was to establish standardized prevalence estimates for CU among adults in the United States.

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METHODS

We performed a cross-sectional analysis using a multihealth system data analytics and research platform (Explorys) developed by IBM Watson Health (Cambridge, MA).[15] Clinical information from electronic medical records, laboratories, practice management systems, and claims systems were matched by using the single set of Unified Medical Language System ontologies to create longitudinal records for unique patients. The data are standardized and curated according to common controlled vocabularies and classifications systems, including International Classification of Diseases, Ninth Revision (ICD-9), Systemized Nomenclature of Medicine—Clinical Terms (SNOMED-CT), Logical Observation Identifiers Names and Codes, and RxNorm.[16-19] At present, the database encompasses 27 participating integrated health care organizations. Over 55 million unique persons representing ~17% of the population across all 4 census regions of the United States are captured. Patients with all types of insurance as well as those who are self-pay are represented. Population counts are reported by the database to the nearest 10, or represented as <10 if between 0 and 10, to prevent patient identification. Human Subjects Committee review was waived by the Feinstein Institute for Medical Research at Northwell Health because there are no identifiers associated with the data.

A case cohort was established by using the diagnosis code for the SNOMED-CT term urticaria, indicated by ICD-9 codes 708.1 (idiopathic urticaria), 708.8 (other specified urticaria), and 708.9 (unspecified urticaria) that was followed by a second diagnosis code at least 6 weeks later for either urticaria or the SNOMED-CT term angioedema, indicated by ICD-9 code 995.1 (angioneurotic edema). This method has been previously validated and shown to have a positive predictive value of 90.4% for identifying cases of CU.[20]

Statistical analysis

We calculated the overall prevalence of CU among patients ≥18 years of age who were active in the Explorys database during 2012-2017, as well as the prevalence of CU within subgroups according to age, sex, and race. Patients were categorized into 1 of 4 race categories: white alone, black alone, other (biracial, Hispanic/Latino, Asian, multiracial, and other), and unknown. Patients who were not white or black were classified as other because of the relatively small number of CU cases within the other race groups. Prevalence estimates are based on records for which age and sex information was available. Direct standardization was used to account for differences in sex and age distributions when comparing CU prevalence across subgroups. The age and sex composition of the 2010 US Census population was used as the standard population, with 5 age groups: 18-29, 30-39, 40-49, 50-59, and ≥60 years.[21] Estimates were age adjusted for comparison between male and female patients, sex adjusted for age group comparisons, and sex and age adjusted for race comparisons. Confidence intervals for crude and standardized prevalences were computed on the basis of the Poisson and gamma distributions,[22] respectively. Standardized prevalences were compared under the assumption that the prevalence ratio has a log-normal distribution. A 2-sided α level of 0.05 was applied to determine statistical significance. All analyses were performed by using SAS version 9.4 (SAS Institute Inc, Cary, NC).

CAPSULE SUMMARY

- Disease burden of chronic urticaria in the United States is poorly understood.
- Over 500,000 people living in the United States are estimated to have chronic urticaria, most of whom are women and adults aged 40-59 years, who might benefit from seeking treatment from a dermatologist.

RESULTS

Table I lists demographic characteristics of adult CU patients in the population-based sample. We identified 69,570 adult patients with CU. The ratio of women to men with CU was 2.7 to 1. CU patients were most frequently white (70.0%).

Crude and standardized group-specific prevalences of CU among adult patients are listed in Table II. We observed an overall standardized point prevalence of 0.23%, or 229.8 (95% confidence interval [CI] 228.0-231.5) CU cases/100,000 adults in the United States. The standardized prevalence was 2-fold greater in women (309.3 [95% CI 306.6-312.1] cases/100,000 adults) than men (145.5 [95% CI 143.4-147.7] cases/100,000 adults, $P < .001$). Standardized prevalence was similar among all age groups and ranged from 0.21% among patients aged 18-29 years and 30-39 years to 0.26% among those aged 40-49 years. Standardized prevalence was highest among patients of the other race category (330.5 [95% CI 323.2-337.8] cases/100,000 adults]), followed by black patients (291.6 [95% CI 285.4-297.9] cases/

Abbreviations used:

CI:	confidence interval
CU:	chronic urticaria
ICD:	International Classification of Diseases
SNOMED-CT:	Systemized Nomenclature of Medicine—Clinical Terms

100,000 adults) then white patients (261.9 [95% CI 259.5-264.3] cases/100,000 adults; $P < .001$).

Age-specific prevalences by sex are listed in Table III. Female patients had a greater prevalence of CU across all age groups. The highest prevalence of CU was observed among women aged 40-49 years (364.0 [95% CI 356.6-371.5] cases per 100,000 adults).

Table I. Demographic characteristics of adults with chronic urticaria (N = 69,570)

Characteristic	n (%)*
Sex	
Female	51,010 (73.3)
Male	18,560 (26.7)
Age, y	
18-29	11,690 (16.8)
30-39	10,540 (15.2)
40-49	11,880 (17.1)
50-59	12,560 (18.1)
≥60	22,900 (32.9)
Race	
White alone	48,700 (70.0)
Black alone	8660 (12.4)
Other†	8090 (11.6)
Unknown	4120 (5.9)

*Sum of group-specific counts might not equal total N because the database rounds counts to the nearest 10.
†Other includes patients whose race was recorded as Hispanic/Latino, Asian, multiracial, or other, as well as patients with ≥2 races on record.

DISCUSSION

In this study, we have estimated overall and group-specific standardized prevalence estimates for CU among adults in the United States. The overall point prevalence of CU is 0.23% (or 230 CU cases/100,000 adults). The standardized prevalence of CU among women was twice that of men. Patients aged 40-49 years had the highest age-specific CU prevalence. Women in this age group had the highest prevalence among all age and sex subgroups.

Epidemiologic studies estimating disease burden for CU are sparse, particularly in the United States. Moreover, there are limitations to the existing studies, which include use of interview or questionnaires not specifically designed to identify CU, self-report of diagnosis, selection and recall biases within samples, or nonstandardization of prevalence estimates to a national reference population. Reports of worldwide prevalence estimates for CU range widely from 0.08% to 3.08%,[23-35] which might be a reflection of these different methods of case cohort identification (ie, self-report of diagnosis vs diagnosis codes) or could be the result of differing sample types (ie, population-based vs single center), study periods, and inclusion criteria (ie, age, insurance type).

In the largest European study, 175,923 adults across 5 countries self-identified their diagnosis of CU.[23] The prevalence of CU was 0.51%, and women had a prevalence that was approximately twice that of men. Although the data in this study were weighted to account for probability sampling, they were not standardized. A questionnaire-based study in Poland included 4897 individuals.[32] The overall prevalence of CU in this population was 0.6%. However, patients who were at least 15 years of age were included in the analysis of this study, and prevalence comparisons may not have been standardized. In the largest American questionnaire-based study, 0.4% of 197,463 adults self-reported having ever been diagnosed with CU.[28] The standardized prevalence among women was over twice that of men. Standardized prevalence was observed to be lowest among those aged 18-24 years and highest in those aged 45-54 years.

Claims analyses have also been applied to establish disease burden of CU. In an Italian analysis involving 14,859 CU patients, the point prevalence in 2013 was estimated to be 0.38%.[29] This study included patients who were at least 15 years of age. In an American claims-based analysis, the 1-year period prevalence of CU was estimated to be of 0.08%.[31] However, this study might have underestimated disease burden by only including patients with commercial insurance. Neither claims analysis standardized estimates to their respective population, which limits the interpretation of true burden. Information on race was not reported. In a Korean analysis that included patients ≥10 years of age, the prevalence of chronic or recurrent urticaria during 5 years was estimated to be 0.38% of the population.[33] The prevalence was highest among patients aged 50-59 years. In a separate Korean claims analysis that included patients of all ages, the prevalence of CU was 3.08%.[34] Those aged 0-9 years and 70-79 years had the highest prevalences. Last, a small study on the claims from a single health organization in Buenos Aires identified 395 adults with CU that yielded a crude point prevalence of 0.34%.[35]

Table II. Crude and standardized group-specific prevalence estimates for chronic urticaria in the United States

Demographic	Urticaria cases, n*	Population size*	Crude prevalence per 100,000 adults (95% CI)	Crude prevalence, %	Standardized prevalence per 100,000 adults (95% CI)†‡	Standardized prevalence, %
Overall population	69,570	29,248,110	237.9 (236.1-239.6)	0.24	229.8 (228.0-231.5)	0.23
Sex						
Female	51,010	16,570,240	307.8 (305.2-310.5)	0.31	309.3 (306.6-312.1)	0.31
Male	18,560	12,677,870	146.4 (144.3-148.5)	0.15	145.5 (143.4-147.7)	0.15
Age, y						
18-29	11,690	5,327,420	219.4 (214.5-223.4)	0.22	213.5 (209.6-217.4)	0.21
30-39	10,540	4,777,460	220.6 (216.4-224.9)	0.22	207.2 (203.2-211.2)	0.21
40-49	11,880	4,432,000	268.1 (263.3-272.9)	0.27	256.3 (251.7-261.0)	0.26
50-59	12,560	4,954,020	253.5 (249.1-258.0)	0.25	246.1 (241.8-250.5)	0.25
≥60	22,900	9,757,210	234.7 (231.7-237.8)	0.23	228.3 (225.3-231.3)	0.23
Race						
White	48,690	17,971,380	270.9 (268.5-273.3)	0.27	261.9 (259.5-264.3)	0.26
Black	8670	2,827,520	306.6 (300.2-313.2)	0.31	291.6 (285.4-297.9)	0.29
Other	8110	2,386,140	339.9 (332.5-347.4)	0.34	330.5 (323.2-337.8)	0.33
Unknown	4120	6,063,120	68.0 (65.9-70.1)	0.07	68.2 (66.1-70.4)	0.07

CI, Confidence interval.
*Sum of group-specific counts might not equal total N because the database rounds counts to the nearest 10.
†Sex comparisons are adjusted for age. Age group comparisons are adjusted for sex. Race comparisons are adjusted for sex and age. The sex and age distribution of the 2010 US Census population was used as the standard population, with 5 age groups: 18-29, 30-39, 40-49, 50-59, and ≥60 years.
‡The reference groups for sex, age, and race comparisons were female, age group 40-49 years, and white, respectively. All comparisons between standardized subgroups were significant with a P value $< .001$, except for age groups 40-49 years and 50-59 years where $P = .0016$.

Table III. Age-specific prevalence of chronic urticaria by sex

	Male		Female	
Age group, y	CU cases, n	Prevalence, CU cases per 100,000 adults	CU cases, n	Prevalence, CU cases per 100,000 adults
18-29	3640	158.9 (153.8-164.1)	8060	265.4 (259.7-271.3)
30-39	2250	114.7 (110.0-119.5)	8290	295.5 (288.2-300.9)
40-49	2720	142.0 (136.7-147.4)	9160	364.0 (356.6-371.5)
50-59	3320	150.4 (145.3-155.6)	9240	336.4 (329.6-343.3)
≥60	6640	154.4 (150.7-158.1)	16,270	298.2 (293.7-302.9)

The P value was <.001 for all age-specific comparisons between male and female patients.
CU, Chronic urticaria.

There are limits which warrant consideration when interpreting the results of our study. We could not capture patients who did not seek care in health systems included in the database. The extent to which our analysis underestimates CU frequency due to this reason is unknown. Although the case cohort was identified by using a previously validated method, use of administrative data for case identification is an imperfect standard that might result in misclassification bias. This study also has several strengths. The prevalence estimate was based on one of the largest and most ethnically diversified population samples in the United States. It is also drawn from patients with all insurance types and self-pay patients across various types of health care settings and from all census regions. For these reasons, we believe these results are generalizable in the United States.

In conclusion, we estimate that >500,000 people living in the United States have CU, most of whom are women and adults aged 40-59 years.

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